The thesis entitled "**Stereoselective Total Synthesis of Paecilomycin E, F and Seimatopolide A along with Development of New Synthetic Methodologies**" has been divided into five chapters.

Chapter I: Describes the Stereoselective total synthesis of peacilomycin E and F.

This Chapter has been divided into two sections.

Section A: Resorcyclic acid lactones: Preview

β-Resorcylic acid lactones (RALs), a group of fungal Secondary polyketide metabolites, are resorcylic acid derivatives containing two parts of β-resorcylic acid unit and the macrocyclic ring unit to form a 14-membered lactone ring. Since the first isolation of radicicol in 1953, more than 30 naturally occurring RALs have been reported. Due to their potential biological activities such as estrogenic, antifungal, cytotoxic, antimalarial, and nematicidal properties and inhibitory activities particularly against ATPases and kinases, organic chemist showed great attention to synthesise these resorcyclic acid lactones (RALs). Consequently several reports on the synthesis and extensive study of the biological properties have been published in the repute journals.

Section B: Streoselective total synthesis of Paecilomycin E and Paecilomycin F.

Recently Wei and co-workers reported the isolation of six new resorcylic acid lactones named **paecilomycins A-F** from the mycelial

solid culture of *Paecilomyces* sp. SC0924. **Paecilomycin E (1)** (**Fig.1**) showed antiplasmodial activity against *Plasmodium falciparum* line 3D7 with IC_{50} values of 20.0 nM and **Paecilomycin F (2)** showed moderate activity against the *P.falciparum* line Dd2 with IC_{50} values of 1.7 μM.

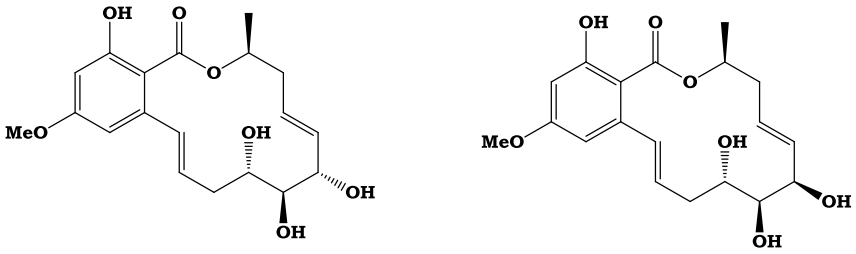
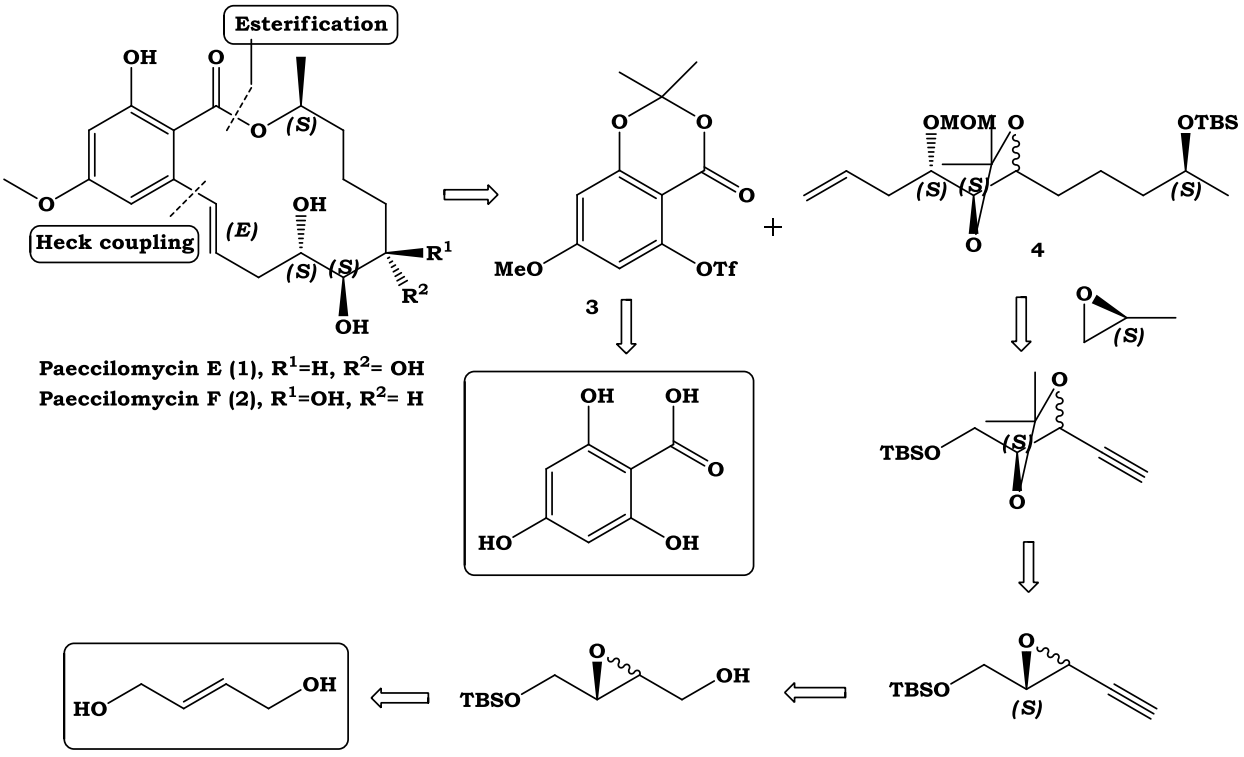


Fig. 1

The structure and biological profiles of **Paecilomycin E (1)** and **Paecilomycin F (2)** prompted us to synthesis these two RALs in an alternative efficient and simple synthetic pathway.

Our retro-synthetic analysis revealed that both peacilomycin E and F could be accomplished from the Heck coupling followed by esterification of the two key fragments, aromatic triflates fragment **3** and C_{11} side chain fragment **4 (Scheme 1)**. The aromatic triflates fragment **3** could be furnished from the 2,4,6- trihydroxy benzoic acid and both the isomer of side chain fragment **4 & 4′** could be accomplished from the opening of (S)- propylene epoxide by alkynes.

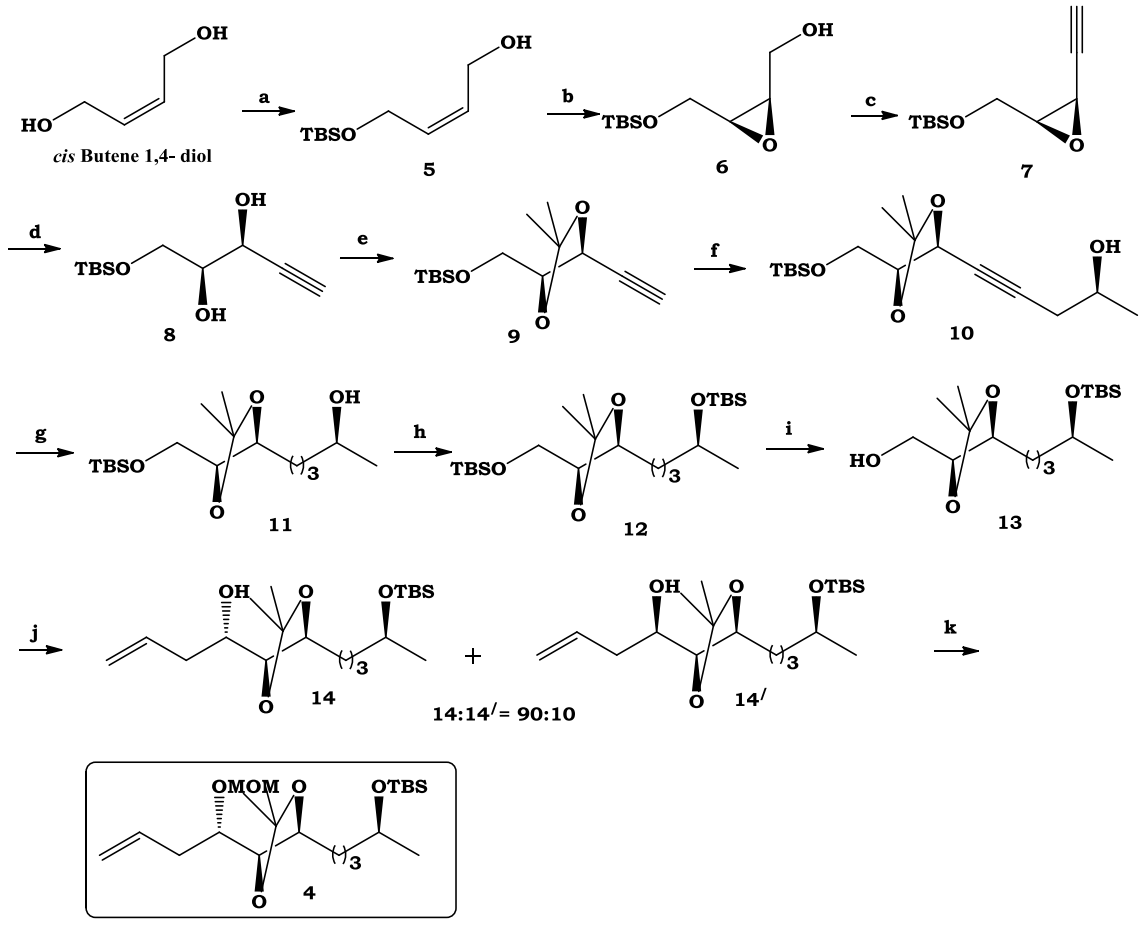
The two isomers of alkynes could be furnished from respective (*cis* and *trans* isomer) butene1,4-diol using Sharpless asymmetric epoxidation protocol followed by regioseletive epoxide dihyroxylation and alkynation.



Scheme 1

The synthesis of C11 side chain fragment **4** (**Scheme 2**) has been started from butene 1,4- diol. For paecilomycin E we started from *cis*-butane 1,2- diol which subjected to mono TBS protection led the mono alcohol **5.** The alcohol **5** was then treated with (-) DIPT under Sharpless asymmetric epoxidation condition to produce epoxide **6**. The epoxy alcohol **6** was then converted to epoxy aldehyde which was treated with Bestmann Ohira reagent to yield alkyne **7**. Regioselective dihydroxylation of epoxy alkyne **7** was led to diol **8** which was

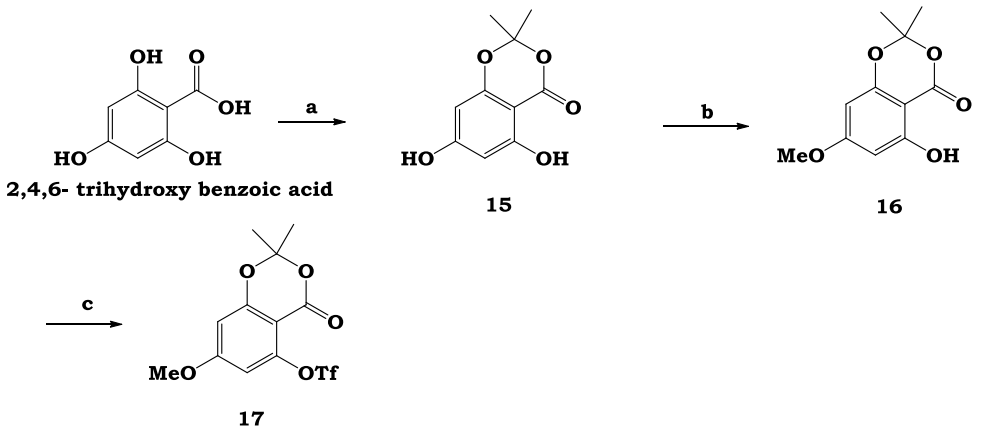
subjected to acetonide protection to furnish the alkyne ether **9**. The opening of (S)- propylene epoxide by alkyne ether **9** was yielded the alcohol **10** which was subjected to reduction of alkyne using hydrogenation protocol led the saturated alcohol **11** followed by TBS protection of alcohol furnished the di-sillyl ether **12**. Selective deprotection of primary TBS protection was accomplished the alcohol **13**. The alcohol **13** was subjected to oxidation to aldehydes followed by Zn mediated allylation of aldehydes was yielded the diastereomeric alcohol **14** in ratio (90:10). The diasteremeric alcohol was the subjected to MOM protection and requisite fragment **4** was separated well.



Scheme 2

Scheme 2: Reagent and conditions: (a) NaH, TBSCl, THF, 0°C to rt, 2h, 95%; (b) $Ti(O^iPr)_4$, (-)DIPT, ^tBuOOH, 4A° MS, CH_2Cl_2, -20°C, 18h, 87%; (c) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C to r.t., 2h, 93%; (ii) Bestmann Ohira reagent (Dimethyl(1-diazo-2-oxopropyl)phosphonate), K_2CO_3, MeOH, 0°C to rt, 85%; (d) $Sc(OTf)_2$, THF/H_2O, 0°C, 30min, 85%; (e) 2,2- DMP, *p*-TSA, 0°C, 91%; (f) *n*BuLi, (S)- propylene epoxide, $BF_3.(OEt)_2$, THF, -78°C, 2h, 82%; (g) Pd-C(10%), H_2, EtOAc, 2h, 96%; (h) TBSCl, imidazole, DMAP (cat.), DMF, 0°C to rt, 1h, 95%; (i) HF.Pyridine, THF, 0°C, 2h, 83%; (j) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C to r.t., 2h, 91%; (ii) Zn, CH_2=CH-CH_2Br, NH_4Cl, THF, -20°C, 4h, 87%; (k) MOMCl, DIPEA, CH_2Cl_2, 0°C to rt, 6h, 89%.

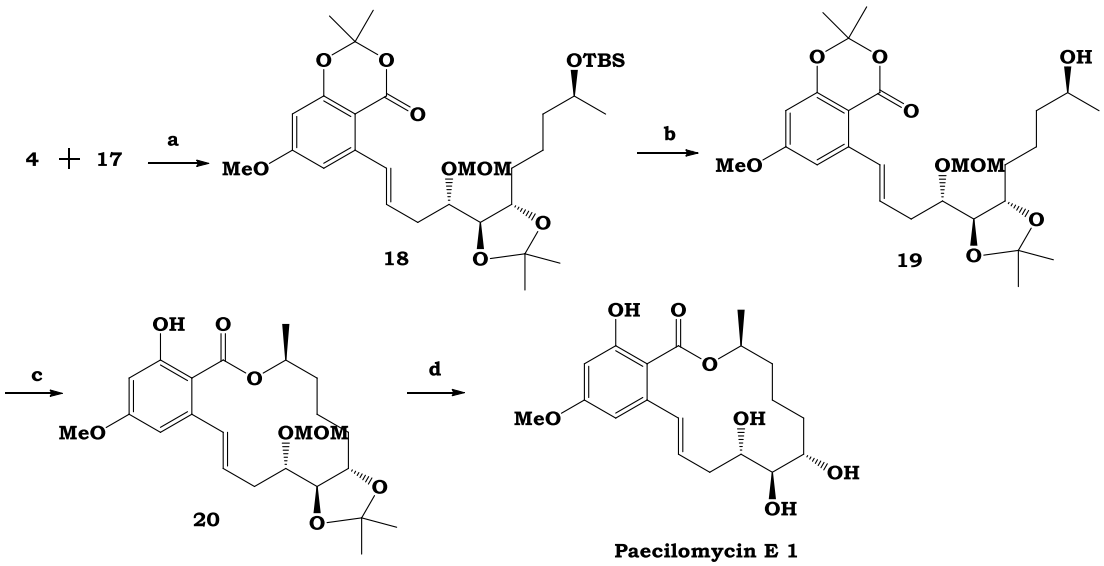
The synthesis of aromatic triflates **3** (**Scheme 3**) commenced from commercially available 2,4,6- trihydroxy benzoic acid which was subjected to acetonide protection followed by regioselective methylation of *p*- hydroxyl group under Mitsunobu's condition was led the phenolic compound **16**. The phenolic compound was then converted to cooreponding triflates **17**.



Scheme 3

Scheme 3: Reagents and conditions: (a) Acetone, $SOCl_2$, DMAP, DCE, 0°C to rt, 4h, 81%; (b) DIAD, PPh_3, MeOH, THF, 0°C to rt, 95%; (c) Tf_2O, Pyridine, 0°C to rt, 92%.

The coupling of two fragment (**Scheme 4**) aromatic triflates **17** and terminal alkene of **4** was performed using Heck coupling protocol to furnish the key precursor **18**. Deeprotection of the sillyl group of **18** to furnish **19** which was subjected to esterification was led to **20**. Finally deprotection of the both protecting group was furnished the peacilomycin E **1**.

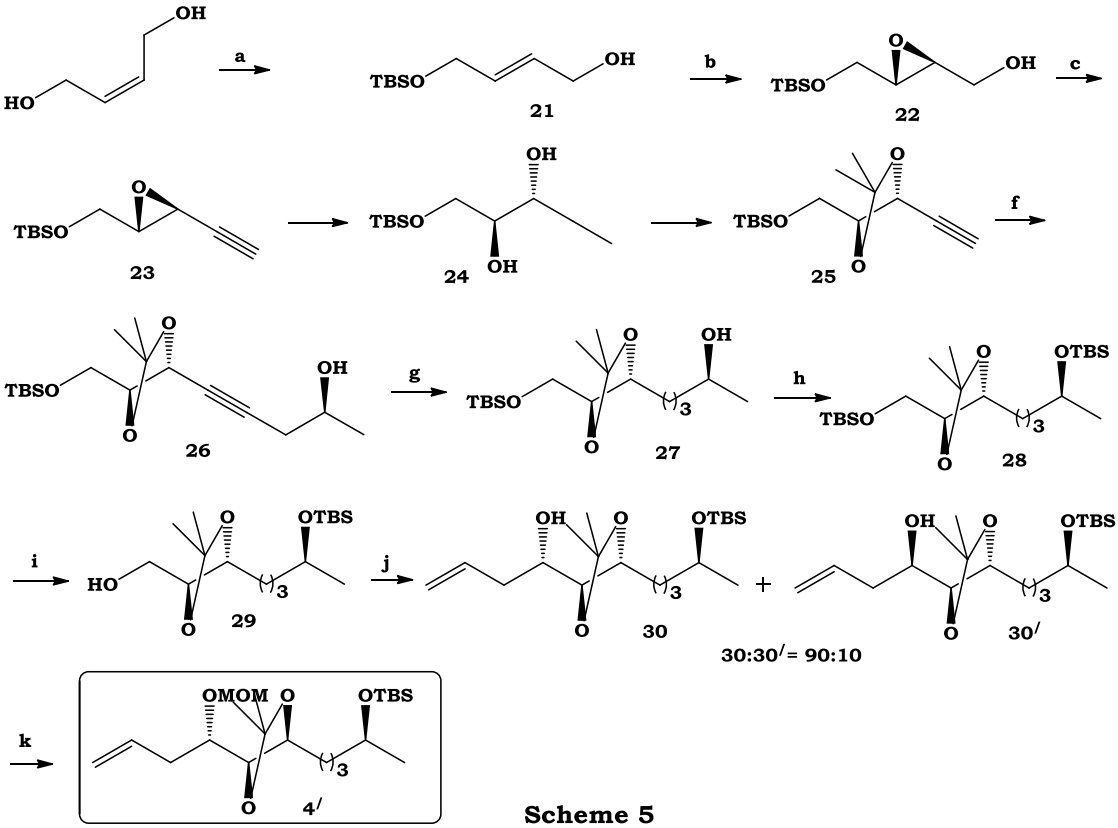


Scheme 4

Scheme 4: Reagents and conditions: (a) $Pd(PPh_3)_2Cl_2$, LiCl, Et_3N, DMF, 120˚C, 10h, 88%; (b) TBAF, THF, 0°C to rt, 90%; (c) NaH, THF/DMF, 0°C to rt, 79%; (d) 2(M) HCl, THF, 10h, 89%.

The synthesis of the side chain fragment for paecilomycin F (**Scheme 5)**, we taken *cis* butene 1,4- diol as starting materials which was subjected to mono TBS protection led the mono alcohol **5** which was converted to *trans* alcohol **21** by oxidation of alcohol to aldehydes and subsequent reduction of aldehydes to alcohol. The alcohol was then treated with (-) DIPT under Sharpless asymmetric epoxidation condition to produce epoxide **22**. The epoxy alcohol was then

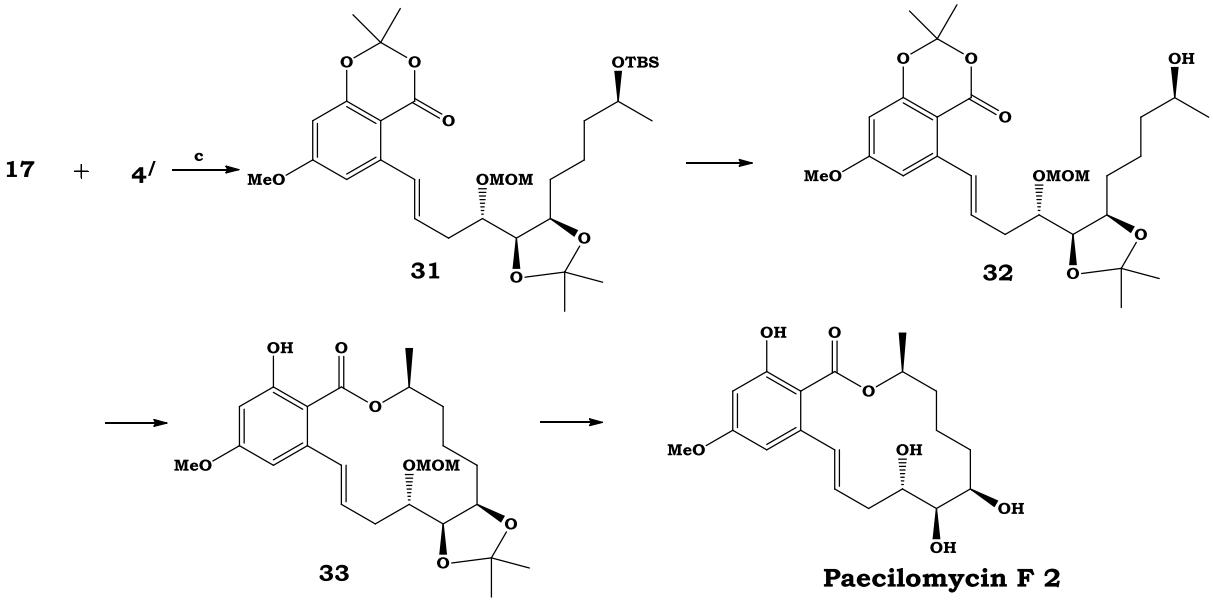
converted to epoxy aldehyde which was treated with Bestmann ohira reagent to yield alkyne **23**. Regioselective dihydroxylation of epoxy alkyne **23** was led to diol **24** which was subjected to acetonide protection to furnish the alkyne ether **25**. The opening of (S)-propylene epoxide by alkyne ether **25** was yielded the alcohol **26** which was subjected to reduction of alkyne using hydrogenation protocol led the saturated alcohol **27** followed by TBS protection of alcohol furnished the di-sillyl ether **28**. Selective deprotection of primary TBS protection was accomplished the alcohol **29**. The alcohol **29** was subjected to oxidation to aldehydes followed by Zn mediated allylation of aldehydes was yielded the diastereomeric alcohol **30** and **30′** in ratio (90:10). The diasteremeric alcohol was the subjected to MOM protection to furnish requisite fragment **4′** which was well separated by column chromatography.



Scheme 5

Scheme 5: Reagent and conditions: (a) (i) NaH, TBSCl, THF, 0°C to rt, 2h, 95%; (ii) PCC, CH_2Cl_2, celite, 0°C to rt, 2h, 91%; (iii) NaBH4, MeOH, 0°C to rt, 2h, 87%. (b) $Ti(O^iPr)_4$, (-)DIPT, ^tBuOOH, 4Aº MS, CH_2Cl_2, -20°C, 18h, 87%; (c) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C to r.t., 2h, 93%; (ii) Bestmann Ohira reagent (Dimethyl(1-diazo-2-oxopropyl)phosphonate), K_2CO_3, MeOH, 0°C to rt, 85%; (d) $Sc(OTf)_2$, THF/H_2O, 0°C, 30min, 85%; (e) 2,2- DMP, *p*-TSA, 0°C, 91%; (f) *n*BuLi, (S)- propylene epoxide, $BF_3.(OEt)_2$, THF, -78°C, 2h, 82%; (g) Pd-C(10%), H_2, EtOAc, 2h, 96%; (h) TBSCl, imidazole, DMAP (cat.), DMF, 0°C to rt, 1h, 95%; (i) HF.Pyridine, THF, 0°C, 2h, 83%; (j) (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C to r.t., 2h, 91%; (ii) Zn, CH_2=CH-CH_2Br, NH_4Cl, THF, -20°C, 4h, 87%; (k) MOMCl, DIPEA, CH_2Cl_2, 0°C to rt, 6h, 89%.

The coupling of two fragment (**Scheme 6**) aromatic triflates **17** and terminal alkene of **4′** was performed using Heck coupling protocol to furnish the key precursor **31**. Deeprotection of the sillyl group of **31** to furnish **32** which was subjected to esterification was led to **33**. Finally deprotection of the both protecting group was furnished the peacilomycin F **2**.



Scheme 6

Scheme 6: Reagents and conditions: (a) $Pd(PPh_3)_2Cl_2$, LiCl, Et_3N, DMF, 120˚C, 10h, 85%; (b) TBAF, THF, 0°C to rt, 93%; (c) NaH, THF/DMF, 0°C to rt, 81%; (d) 2(M) HCl, THF, 10h, 87%.

Chapter II: Describes the Stereoselective synthesis of seimatopolide A. This Chapter has been divided into two sections.

Section A: Macrolides: Preview

The peroxisome proliferator-activated receptors (PPARs) are the nuclear hormone receptors and they are activated by specific ligands. PPARγ is said to be potential target for the treatment of type II diabetes, inflammatory disease, and some type of cancer. Polyhydroxylated macrolides isolated from fungal sources has attracted much attention recently due to their biological properties such as antimalarial, antibacterial activities and cholesterol biosynthesis inhibitor. Seimatopolides A (**34**) and B (**35**) are such new polyhydroxylated macrolides, recently isolated from an EtOAc extract of Seimatosporium discosioides culture medium.

Section B: Streoselective total synthesis of Seimatopolide A.

In 2012, Lee and co-workers isolated two new polyhydroxylated macrolides seimatopoolide A (**34**) and seimatopolide B (**35**) (**Fig. 2**) from the ethyl acetate extract of the fungal culture medium of *Seimatosporium discosioides*. Seimatopolides A (**34**) and B (**35**) activated peroxisome proliferator activated receptor (PPAR)- γ with EC_{50} values of 1.15 and 11.05 μM, respectively. Seimatopolide A also

moderately reduced the expression of two gluconeogenic genes, glucose-6-phosphatase (G6Pase) and phosphoenol- pyruvate carboxykinase (PEPCK), suggestsing that the compound is a possible therapeutic candidate as an antidiabetic drug. These structural and biological profiles attracted us for the total synthesis of this compound. Herein we report the stereoselective total synthesis of seimatopolide A (**34**) through an alternative simple and efficient route.

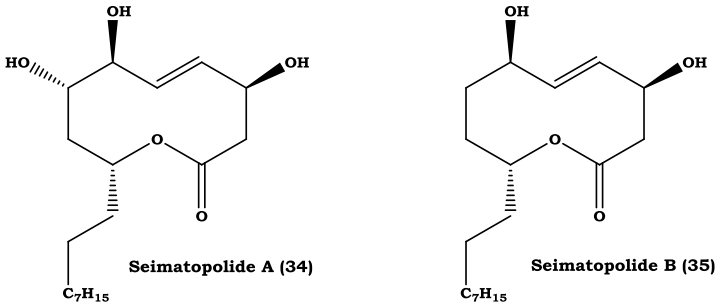
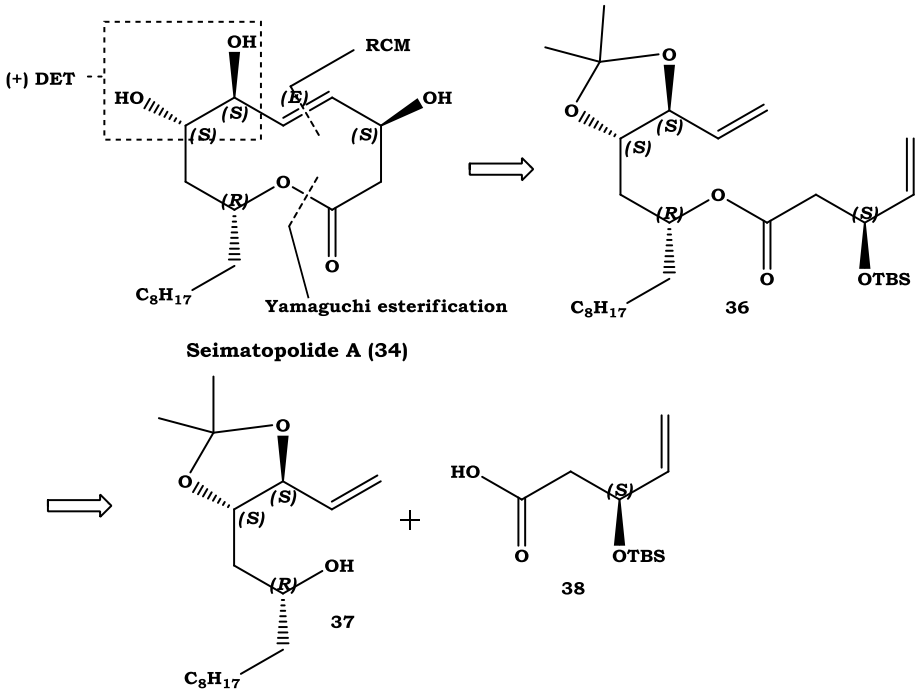


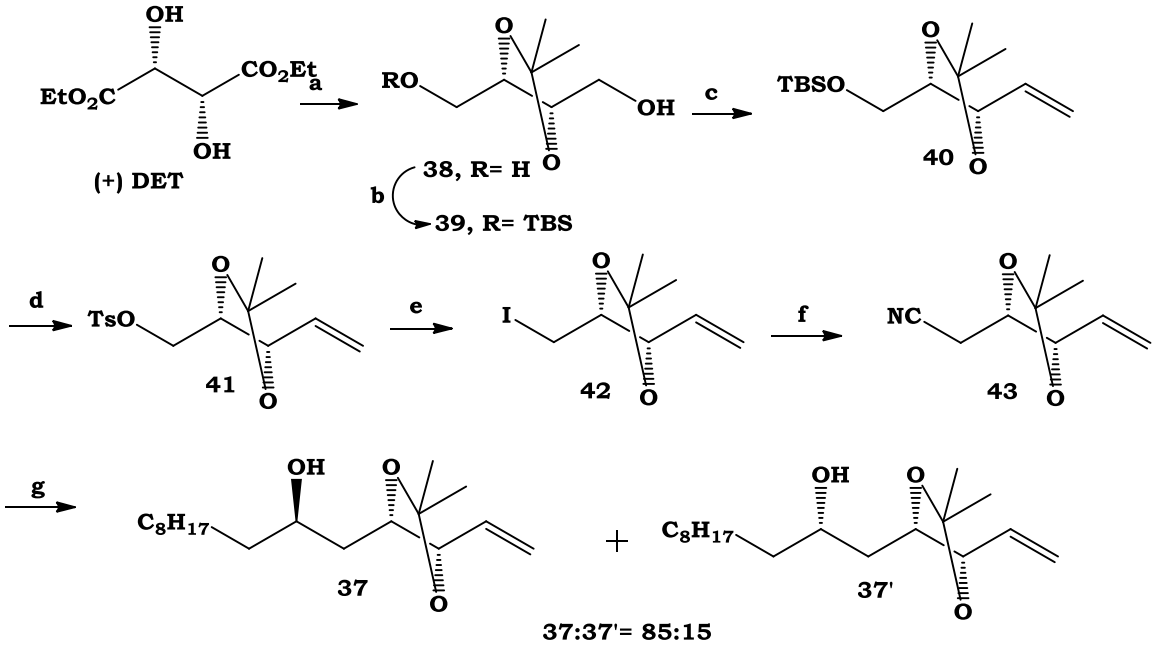
Fig. 2

The retro- synthetic analysis for seimatopolide A **24** (**Scheme 7**) revealed that the compound could be prepared by ring closing metathesis of the diene precursor **36** which could be obtained by the Yamaguchi esterification of the two key fragments, alcohol fragment **37** and acid fragment **38**.



Scheme 7

The synthesis of the alcohol fragment **37** has been started (**Scheme 8**) from (+) diethyl tartrate which was subjected to acetonide protection with 2, 2- DMP in the presence of pTSA in CH_2Cl_2 followed by reduction of the ester groups with DIBAL-H to afford the diol **39**. The diol was subjected to monoprotection with TBSCl in the presence of NaH in THF to produce the alcohol **40**. The oxidation of primary alcohol, **40** under Swern oxidation conditions led to the corresponding aldehyde which was subsequently reacted with one carbon ylide to furnish the olefin **41**. Desilylation of **41** to form primary alcohol and followed by tosylation furnished the tosylated compound **42**.

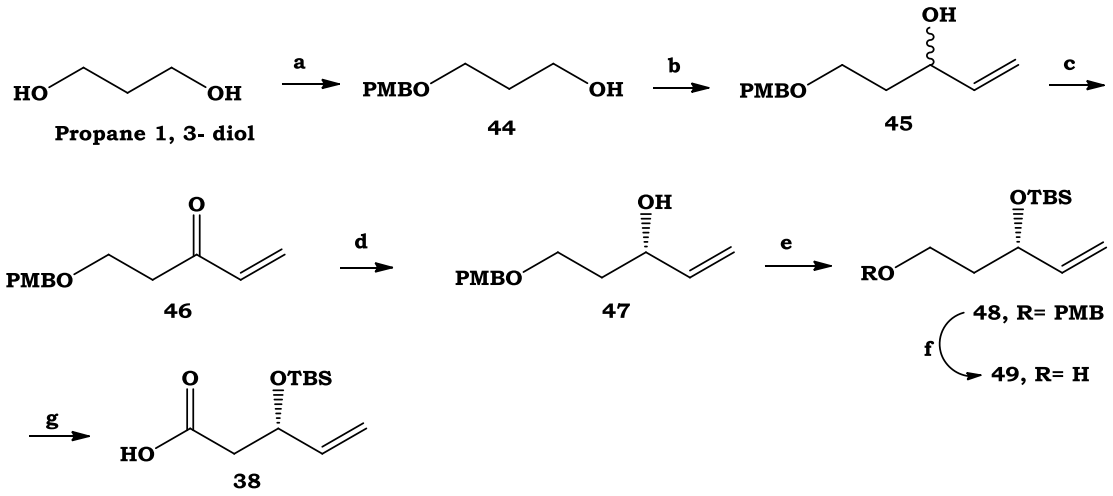


Scheme 8

Scheme 8. Synthesis of fragment **37**. Reagent and Conditions: (a). (i) 2,2- DMP, pTSA, CH_2Cl_2, 0°C to r.t., 6h, 86%. (ii) DIBAL-H, CH_2Cl_2, -78°C, 30 min, 92%. (b). NaH, TBSCl, THF, 0°C to r.t., 2h, 89%. (c). (i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C to r.t., 2h, 93%. (ii) $CH_3PPh_3^+Br^-$, *n*BuLi, THF, -78°C to r.t., 4h, 71%. (d). (i) TBAF, THF, 0°C to r.t. 6h, 88%. (ii) TsCl, Et_3N, DMAP (cat.), CH_2Cl_2, 0°C to r.t., 2h, 91%. (e) NaI, acetone, reflux, 3h, 87%. (f) NaCN, DMSO, 0°C to r.t., 6h, 92%. (g). (i) DIBAL-H, CH_2Cl_2, -78°C, 30 min, 90%. (ii) $C_9H_{19}MgBr$, diethyl ether, -20°C, 4h, 82%.

The treatment of NaCN/NaI(cat.) to the tosylated compound **41** in acetone did not furnished the cyanated compound. Next, the tosylated compound **41** was subjected to iodination to afford the iodo compound **42** which underwent cyanation using NaCN in DMSO to generate the cyanated compound **43**. The cyano group was then converted to aldehydes (90% yield) using DBAL-H in CH_2Cl_2 and subsequently the aldehyde was treated with nine cabon magnesium salt (generated from Mg and $C_9H_{19}Br$ in ether) for Grignard reaction to furnish the alcohol

37 along with its separable diastereoisomer in 85:15 ratio. The desired alcohol **37** has been utilized for the subsequent steps.

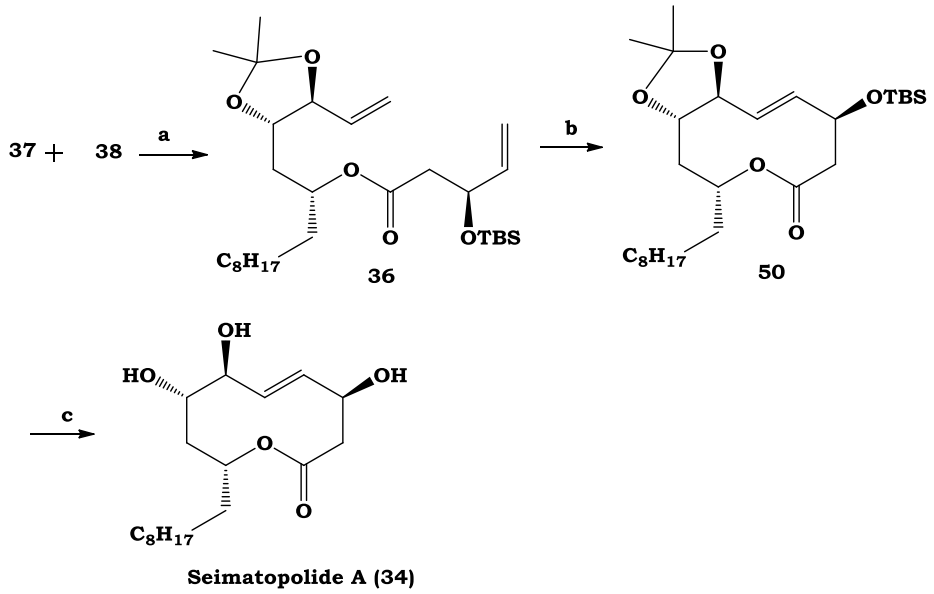


Scheme 9

Scheme 9. Synthesis of fragment 5. Reagent and Conditions: (a) NaH, THF, 0°C to r.t., 6h, 86%; (b). (i) PCC, 4A° MS, CH_2Cl_2, 0°C to r.t., 2h, 91%; (ii) CH_2=CHMgBr, THF, 0°C to r.t., 2h, 83%; (c) IBX, DMSO/CH_2Cl_2, r.t., 91%; (d) CBS reduction, S- (-)- 2 methyl oxaborolidine $BH_3.Me_2S$, THF, -30°C, 2h, 93%; (e) TBSCl, imidazole/ DMAP (cat.), DMF, 0°C to r.t., 3h, 95%; (f) DDQ, CH_2Cl_2/H_2O, 0°C to r.t., 4h, 91%; (g) TEMPO/BAIB, CH_2Cl_2/H_2O, 0°C to r.t., 5h, 89%.

The synthesis of requisite acid fragment **38** was started from commercially available 1,3- propane diol (**Scheme 9**). The monoprotection of the diol using 4-methoxy benzyl chloride led to monoproteted alcohol **44**. The primary alcohol **44** was then subjected to oxidation to aldehydes which was reacted with vinyl magnesium bromide to lead the secondary alcohol **45**. The alcohol **45** was then converted to vinyl ketone **46** using IBX. Enantioselective reduction of this vinyl ketone **46** using Corey- Bakshi- Shibata reduction afforded the secondary alcohol **47**. The alcohol was then subjected to TBS

protection to produce the silyl ether **48**. Deprotection of PMB ether was achieved using DDQ to furnish the primary alcohol **49**. Finally the oxidation of alcohol to acid **38** was accomplished using TEMPO/BAIB.



Scheme 10

Scheme 10. Coupling of fragments **37** and **38** to synthesise seimatopolide A, Reagent and Coonditions: (a) **38**, 2,4,6- trichlorobenzoyl chloride, Et_3N, CH_2Cl_2, 0°C to r.t., 1h, 88%, then **37**, DMAP, toluene, r.t., 3h, 86%. (b) Grubbs 2nd generation catalyst 20 mol%, CH_2Cl_2 reflux, 12h, 87%. (c) TFA, CH_2Cl_2, 0°C to r.t., 10h, 81%.

Having both the fragments, alcohol **37** and acid **38** in hand, they were subjected to esterification (**Scheme 10**) under Yamaguchi reaction condition to lead the ester precursor **36**. The ester precursor was then treated with 2nd generation Grubbs' catalyst to furnish the ring closing metathesis to produce the macrolide **50**. Finally, both the protecting groups, acetonide and TBS were deprotected simultaneously to give the seimatopolide A (**34**). All the spectroscopic (^1H, ^{13}C NMR and Mass)

data of synthetic seimatopolide A (**34**) were in full agreement with the natural product.

In conclusion we have achieved the total synthesis of natural seimatopolide A through an alternative and efficient approach starting from relatively inexpensive (+) diethyl tartrate and propane 1,3- diol by applying regieoselective Grignard reaction, CBS reduction , ring closing metathesis reactions and Yamaguchi easterification.

Chapter III: Development of methodology to the synthesis of substituted pyrrole.

This Chapter divided into three sections.

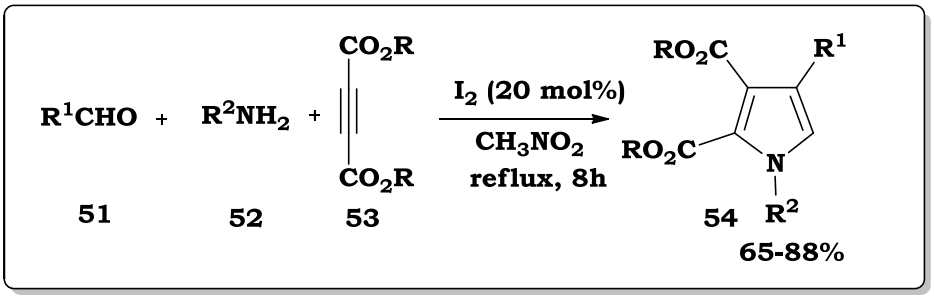
Section A: Introduction

Pyrrole derivatives are the important heterocyclic as they are structural elements of various bioactive natural products such as chlorophyll, bile pigments, heme and vitamin B_{12}. The pyrrole ring is also the structural unit of different drugs having anticancer, antitumor, antibacterial and immune suprresion activities. Several pyrrole derivatives are cholesterol lowering agent (atorvastatin or lipitor) and HIV fusion inhibitors. In addition they are flexible intermediates for transformation into the valuable bioactive heterocyclic system. Pyrrole derivatives are also applied for the preparation of semiconducting and fluorescence materials. Consequently a wide range of methods have been discovered for the synthesis of pyrroles using various metal salts (Pd, Ni, Fe, Cu, Zn, Mg

etc). However these methods suffer from several drawbacks such as, use of toxic metals, tedious experimental procedure, and unsatisfactory yield. Recently synthesis of pyrroles applying multi-component reaction (MCR) strategy attracts much attention to chemist as in MCR strategy combination of three or more starting materials in single synthetic operation provide us high atom economy and bond forming efficiency without isolation and purification of any intermediate which in turn minimise the waste, labour and cost. Herein we described metal free one pot synthesis synthesis of substituted pyrroles.

Section B: A simple and efficient metal-free synthesis of tetrasubstituted pyrroles by iodine catalyzed four component coupling reactions of aldehydes, amines, dialkyl acetylenedicarboxylates and nitromethane.

In continuation of our works on the development of useful novel synthetic methodologies, we have discovered that the four component coupling of aldehydes **51**, amines **52**, dialkyl acetylenedicarboxylates **53** and nitromethane in the presence of molecular iodine as a catalyst afforded the corresponding 1, 2, 3, 4- tetrasubstituted pyrroles **54** under reflux (**Scheme 11**).



Scheme 11

The reaction of benzaldehyde, aniline, dimethyl acetylenedicarboxylate was initially carried out in nitromethane using different catalysts. Iodine (20 mol %) was found to be most effective to catalyze the reaction under reflux. The yield of the products was 84% in 8h. At room temperature or in absence of any catalyst the yields were very low even after 24h.

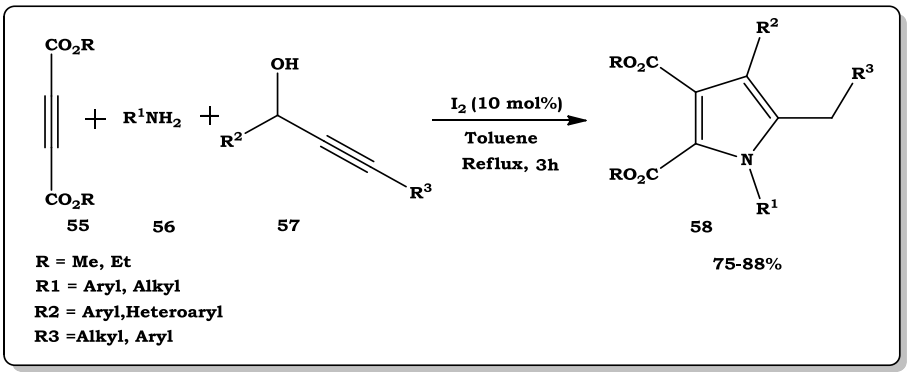
With optimized a series of 1, 2, 3, 4- tetrasubstituted pyrroles were subsequently prepared from various aldehydes, amines and dialkyl acetylenedicarboxylates following the above conditions. Both aromatic and heteroaromatic aldehydes with different substituents were utilised. The aromatic aldehydes contained electron- donating as well as electron- withdrawing groups. However, with an aliphatic aldehyde only a trace amount of product was detected. On the other hand, in the case of amines, both aromatic and aliphatic substrates underwent the conversion smoothly. The pyrrols were efficiently prepared by using dimethyl and diethyl acetylenedicarboxylates. The conversion was completed only in 8h and the products were formed in high yields (65-90%). Nitromethane was used as a reagent and also as a solvent. When nitroethane was used instead of nitromethane the products were formed in trace amount. The structure of the prepared pyrroles were established from their spectral (IR, ^{1}H and ^{13}C NMR and MS) and analytical data.

In conclusion, we have developed a simple, efficient, high-yielding and cost-effective synthesis of 1, 2, 3, 4- tetrasubstituted pyrroles by direct

four component coupling reaction of aldehydes, amines, dialkyl acetylenedicarboxylates and nitromethane using iodine as a catalyst.

Section B: One pot synthesis of penta-substituted pyrroles from propargylic alcohols, amines and dialkyl acetylenedicarboxylates; tandem amination, propygylation and cycloisomerization catalysed by molecular Iodine.

As part of our research on the development of useful synthetic methodologies, we have discovered that the three component coupling of propargylic alcohols **57**, amines **56** and dialkyl acetylenedicarboxylates **55** in the presence of molecular iodine as a catalyst in toluene afforded the corresponding pentatetrasubstituted pyrroles **58** under reflux condition (**Scheme 12**).



Scheme 12

When the reaction mixture (secondary propargylic alcohol derived from the benzaldehyed and phenyl acetylene, dimethyl acetylene dicarboxylate and aniline) was treated with 10 mol% of iodine in toluene under reflux for 3h the expected pyrrole was formed in 88% yield. This is the best result in comparison to other catalysts investigated in the present reaction.

With the optimised reaction conditions, a series of pentasubstituted pyrroles were subsequently synthesised from various secondary propargylic alcohols and amines in excellent yields.

The structure the products were established from their spectral (IR, ^{1}H and ^{13}C NMR and ESIMS) and analytical data.

In conclusion, we have developed a simple and efficient iodine catalysed method for the synthesis of fully substituted pyrroles directly from amines, dialkyl acetylenedicarboxylates and propargylic alcohols in excellent yields. A large number of functional group tolerances, operational simplicity, minimal waste generation (only water generated as by-product) and use of cheap catalyst are main advantages of this method.

Chapter IV: Development of synthetic methodology applying Baylis-Hillman adducts

This Chapter divided into two parts

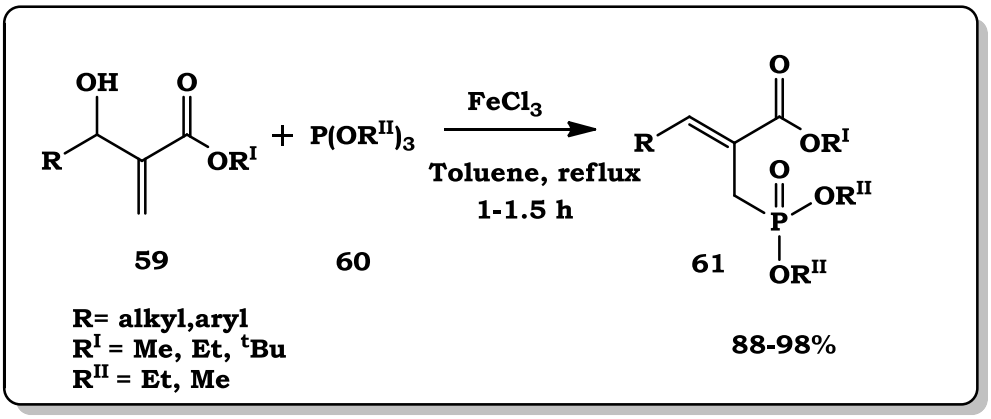
Section A: Baylis- Hillman adduct: an preview

Baylis-Hillman adducts are important precursors for the stereoselective synthesis of various multifunctional molecules. They have been widely employed for the preparation of several natural products, their analogues and other bioactive compounds. However, their utility for the preparation of allyl phosphonates are limited. Allyl phosphonates are important bioactive compounds. They exhibit interesting antimicrobial and antimalarial properties. They are also

useful precursors for the synthesis of various valuable organic compounds.

Section B: A simple and advantageneous stereoselective one pot synthesis of (*Z*)-allyl phosphonates starting from Baylis-Hillman adducts.

As part of our research on the applications of Baylis-Hillman reaction we have observed that the adduct, 3-hydroxy-2-methylene-alkanoates **59** when treated with $FeCl_3$ and trialkyl phosphites **60** in toluene under reflux, were directly converted into the corresponding (*Z*)-allyl phosphonates **61** (**Scheme 13**).



Scheme 13

Finally a series of allyl phosphonates were prepared from different Baylis-Hillman adducts containing ester moiety and $P(OEt)_3$ applying optimized reaction condition. The present method is highly stereoselective only the (*Z*)-allyl phosphonates were obtained exclusively from the adducts derived from aromatic, aliphatic and heteroaromatic aldehydes. The structures of the products were

established by comparison of their spectral data (IR, ^{1}H, ^{13}C NMR and HRMS) with those reported for the known or related compounds.

In conclusion, we have developed a simple and efficient method for the synthesis of (*Z*)- allyl phosphonates from the Baylis-Hillman adducts by treatment with $FeCl_3$ and trialkyl phosphites. The direct conversion of the adducts, convenient experimental procedure, application of less expensive reagents, impressive yields and excellent stereoselectivity are the advantages of the present method.

Chapter V: Multicomponent synthesis of propargyl-1,2,3-triazoles.

This section divided into two sections.

Section A: 1,2,3-triazoles: Preview

1,2,3-Triazoles are highly important on account of their medical uses. They are occasionally found in various orally administrated drugs. They behave as light activatable DNA cleaving agents and potassium channel activators. They are also applicable in material science. Some of these compounds are used as building blocks for the preparation of bioactive molecules. Additionally, they are employed as ligands in transition metal catalysis. Acetylenic compounds, on the other hand, are valuable in biochemistry and material system. Thus, the preparation of triazoles having alkynyl moiety is a useful task in organic synthesis. Here, we report a simple synthesis of propargyl-1,2,3- triazoles involving the coupling of three substrates in one pot.

To the best of our knowledge, there is no report of the multicomponent synthesis of these compounds.

Section B: First Multi Component Synthesis of Propargyl-1,2,3-triazoles.

As part of our ongoing research on the development of useful synthetic methodologies, we have now discovered that the treatment of benzotriazoles **62** with aldehydes **63** and alkynes **64** in the presence of a catalytic amount of zinc bromide in toluene afforded the corresponding propargyl-1,2,3-triazoles **65** under reflux conditions (**Scheme 14**).

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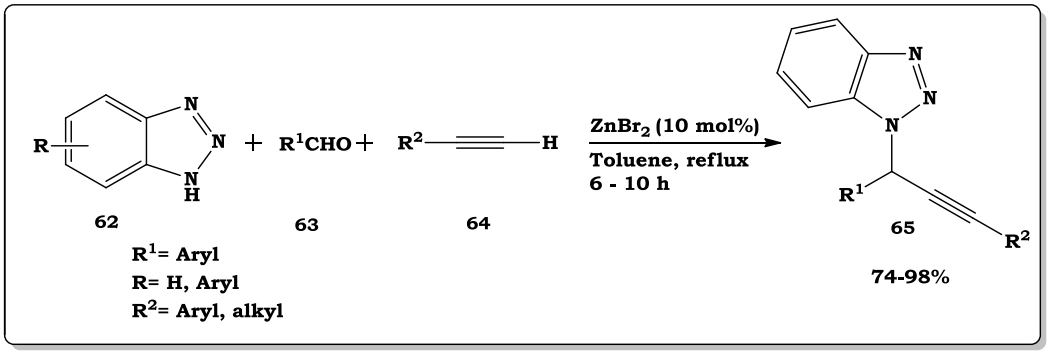

Scheme 14

The conversion was found to be most effective when it was carried out in the presence of zinc bromide in toluene under reflux. Following the optimized reaction conditions, a series of propergyl-1,2,3-triazoles were prepared by zinc bromide catalyzed three-component reaction of benzotriazoles, aldehydes, and alkynes in toluene under reflux. Various benzotriazoles, aldehydes and alkynes has been applied for the preparation of propergyl-1,2,3-triazoles.

In conclusion, we have developed for the first time a simple multicomponent synthesis of propargyltriazoles involving the coupling of benzotriazoles, aldehydes, and alkynes in one pot using zinc bromide as a catalyst.

The research work described in this thesis has been published in the following journals.

1. Stereoselective total synthesis of Peacilomycin E & F, **Nisith Bhunia**; Biswanath Das, (*Communicated to Eur. J. org. chem.* 2013.
2. Concise total synthesis of Seimatopolide A, **Nisith Bhunia**; Biswanath Das, (*Communicated to Tetrahedron Letter*s, 2013.)
3. One-Pot Synthesis of Pentasubstituted Pyrroles from Propargylic Alcohols, Amines and Dialkyl Acetylenedicarboxylates; Tandem Amination, Propargylation and Cycloisomerization Catalyzed by Molecular Iodine, **Nisith Bhunia** and Biswanath Das**,** ***Synthesis*****,** 2013**,** *45,* 1045-1050**.**
4. A Simple and Efficient Metal-Free Synthesis of Tetrasubstituted Pyrroles by Iodine-Catalyzed Four-Component Coupling Reaction of Aldehydes, Amines, Dialkyl Acetylenedicarboxylates, and Nitromethane , Das Biswanath; **Bhunia Nisith**; Lingaiah Maram, ***Synthesis*****,** 2011, *21*, 3471-3474.
5. The First Multicomponent Synthesis of Propargyl-1,2,3-triazoles: Das Biswanath; **Bhunia Nisith**; Lingaiah Maram; ***Synthesis***, 2011, *16*, 2625-2628.
6. Simple advantageneous stereoselective synthesis of (*Z*)- allyl phoosphonates starting directly from Baylis-Hillman adducts, Biswanath Das; **Nisith Bhunia**; Damodar Kongara, ***Synth. Commun***, 2012, *42*, 2479- 2489.

(**Supervisor: Dr. Biswanath Das)